REMARKS-General

1. The newly drafted independent claim 23 incorporates all structural limitations of the original claim 1 and includes further limitations previously brought forth in the disclosure. No new matter has been included. All new claims 23-44 are submitted to be of sufficient clarity and detail to enable a person of average skill in the art to make and use the instant invention, so as to be pursuant to 35 USC 112.

Response to Rejection of Claims 1-22 under 35USC112

2. The applicant submits that the newly drafted claims 23-44 particularly point out and distinctly claim the subject matter of the instant invention, as pursuant to 35USC112.

Regarding to Rejection of Claims 1-4, 6-14, 16-19, and 22 under 35USC102

3. Pursuant to 35 U.S.C. 102, "a person shall be entitled to a patent unless:

(b) the ***invention*** was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.

In view of 35 U.S.C. 102(b), it is apparent that a person shall **not** be entitled to a patent when his or her **invention was patent** in this country more than one year prior to the date of the application for patent in the United States.

4. However, the Pastinen et al. and the instant invention are **not the same invention** according to the fact that the Pastinen does not read upon the instant invention and the independent claim 23 of the instant invention does not read upon the Pastinen too. Apparently, the instant invention, which discloses a method for genetic analysis by **using 3' terminal labeled primers**, should not be the same invention as the Pastinen which discloses a specific tool for DNA analysis and diagnostics on oligonucleotide arrays.

5. According to the instant invention, the 3' terminal labeled primer is a primer that has 3' –OH moiety ready for polymerization. The last nucleotide residue at the 3' terminal of the primer is dNMP. It is different from the sequencing technology that uses

ddNTP for termination of primer extension. When a ddNTP, either labeled or not labeled, is incorporated, the reaction is terminated as ddNTP does not have 3' –OH moiety. The use of ddNTP is the fundamental basis for sequence analysis, a method invented by Sanger who was awarded his second Nobel Prize due to this breakthrough contribution.

6. The applicant respectfully submits that Pastinen fails neither suggest nor anticipate the following distinctive features:

(i) The claiming elements of a process claim are the acts in the steps included, Pastinen fails to anticipate the elements of (a) formation of the nucleic acid target sequence; (b) formation of the 3' terminal labeled primer; (c) formation of primer extension mixture under primer extension reaction conditions; (d) subjection of said primer extension with polymerases; and (e) separation of said extended products with labels integrated from the extended products without labels and from the un-extended primers as claimed in the claim 23 as a whole. Pastinen merely suggests steps of minisequencing on a primer array without teaching any detail technology of how to reduce practice of 3' terminal labeled primer for primer extension. Pastinen provides no substantial steps of how to do it. Moreover, a mere description of the 3' terminal does not equivalent to the detection method as claimed in the instant invention.

(ii) The difference between single base extension (in solution or in solid phase) and regular sequence technology is that one exclusively use ddNTP and another use the mixture of dNTPs and ddNTP. The role of ddNTP in both single base extension and in sequence analysis is the same, serving as a terminator to stop primer extension as there is no free 3' –OH available for polymerization anymore.

(ii) For the 3' terminal labeled primer extension, the presence of 3' –OH is mandatory. After our initial publication in 2001, there are more than 10 scientific papers published in international journals using the 3' terminal modified primers for mutation detection. This new strategy can be well used in single nucleotide polymorphism and other kind of mutations.

Response to Rejection of Claims 5, 15, and 18-19 under 35USC103

7. The Examiner rejected claim 5 over Pastinen et al. in view of Goelet et al., claim 15 over Pastinen et al. in view of Cohen et al., and claims 18-19 over Pastinen et al. in view of Ugozzoli et al. Pursuant to 35 U.S.C. 103:

"(a) A patent may not be obtained thought the invention is **not identically** disclosed or described as set forth in **section 102 of this title**, if the **differences** between the subject matter sought to be patented and the prior art are such that the **subject matter as a whole would have been obvious** at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

In view of 35 U.S.C. 103(a), it is apparent that to be qualified as a prior art under 35USC103(a), the prior art must be cited under 35USC102(a)~(g) but the disclosure of the prior art and the invention are not identical and there are one or more differences between the subject matter sought to be patented and the prior art. In addition, such differences between the subject matter sought to be patented **as a whole** and the prior art are obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains.

8. In other words, the differences between the subject matter sought to be patent as a whole of the instant invention and Pastinen which is qualified as prior art of the instant invention under 35USC102(b) are obvious in view of Goelet, Cohen, and Ugozzoli at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains.

9. However, Pastinen fails to anticipate the newly drafted claims 23-44 that the claiming elements of a process claim are the acts in the steps including: (a) formation of the nucleic acid target sequence; (b) formation of the 3' terminal labeled primer; (c) formation of primer extension mixture under primer extension reaction conditions; (d) subjection of said primer extension with polymerases; and (e) separation of said extended products with labels integrated from the extended products without labels and from the un-extended primers as claimed in the claim 23 as a whole.

10. The Examiner appears to reason that since Pastinen teaches a specific tool for DNA analysis and diagnostics on oligonucleotide arrays, it would have been obvious to one skilled in the art to modify the primer extension. But this is clearly **not** a proper basis for combining references in making out an obviousness rejection of the present claims. Rather, the invention must be considered as a whole and there must be something in the reference that suggests the combination or the modification. *See Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick*, 221 U.S.P.Q. 481, 488 (Fed. Cir. 1984) ("The claimed invention must be considered as a whole, and the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination"), *In re Gordon*, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984), ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.") *In re Laskowski*, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989), ("Although the Commissioner suggests that [the structure in the primary prior art reference] could readily be modified to form the [claimed] structure, "[t]he mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.")

11. In any case, even combining Pastinen, Goelet, Cohen, and Ugozzoli would not provide the invention as claimed -- a clear indicia of nonobviousness. *Ex parte Schwartz*, slip op. p.5 (BPA&I Appeal No. 92-2629 October 28, 1992), ("Even if we were to agree with the examiner that it would have been obvious to combine the reference teachings in the manner proposed, the resulting package still would not comprise zipper closure material that terminates short of the end of the one edge of the product containing area, as now claimed."). That is, modifying Pastinen with Goelet, Cohen, or Ugozzoli, as proposed by the Examiner, would not provide the use of 3' terminal labeled primer extension for genetic analyses.

12. Applicant believes that neither Pastinen, Goelet, Cohen, nor Ugozzoli, separately or in combination, suggest or make any mention whatsoever of using the 3' terminal labeled primer extension for genetic analyses as recited in claim 23.

13. Applicant believes that for all of the foregoing reasons, all of the claims are in condition for allowance and such action is respectfully requested.

The Cited but Non-Applied References

14. The cited but not relied upon references have been studied and are greatly appreciated, but are deemed to be less relevant than the relied upon references.

15. In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of the objection are requested. Allowance of claims 23-44 at an early date is solicited.

16. Should the Examiner believe that anything further is needed in order to place the application in condition for allowance, he is requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Raymond Y. Chan
Reg. Nr.: 37,484
108 N. Ynez Ave.
Suite 128
Monterey Park, CA 91754
Tel.: 1-626-571-9812
Fax.: 1-626-571-9813

CERTIFICATE OF MAILING

I hereby certify that this corresponding is being deposited with the United States Postal Service by First Class Mail, with sufficient postage, in an envelope addressed to "Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on the date below.

Date: June 22, 2004

Signature:
Person Signing: Raymond Y. Chan